2:30 p.m.

821-3 Evaluation of Beta-Blocker Dose in Community-Based Treatment of Heart Failure

Michael B. Fowler, Sandra R. Lottes, Jeanenne J. Nelson, Mary Ann Lukas, Edward M. Gilbert, Barry Greenberg, Barry M. Massie, William T. Abraham, Joseph A. Franciosa, and the COHERE Participant Physicians, GlaxoSmithKline Pharmaceuticals, Philadelphia, PA

Background: Randomized clinical trials (RCT) are performed in a very different environment from community practice. Heart failure patients in the community tend to be older, have more comorbidities and are not cared for by the teams of heart failure specialists who recruit patients into RCT, which may be especially important when beta-adrenergic blocking drugs are prescribed to patients with heart failure.
Methods: In order to explore these prescribing effects we determined the dose of carvedilol at end-titration in 4,113 patients in the practice setting and related this to physician type (cardiologists vs. non-cardiologists), heart failure severity, and the risks of hospitalization and death.
Results: Dose achieved was not related to patients' age, sex, race, history of diabetes or other major demographic/clinical factors. The table shows factors that are influenced by dose.

Patient Characteristics and Outcomes	Carvedilol dose at end-titration (mg bid)					
	0 mg	3.125 mg	6.25 mg	12.5 mg	25 mg	50 mg
No. Patients	386	416	722	759	1672	158
Dose distribution in NYHA I patients (n=445)	7%	7%	17%	17%	46%	5%
Dose distribution in NYHA II patients (n=2099)	9%	9%	16%	18%	43%	4%
Dose distribution in NYHA III patients (n=1390)	11%	11%	18%	19%	38%	3%
Dose distribution in NYHA IV patients (n=131)	5%	18%	30%	21%	23%	4%
Dose distribution in cardiologists' patients (n=2994)	10%	8%	14%	17%	47%	4%
Dose distribution in non-cardiologists' patients (n=1119)	7%	17%	27%	21%	24%	4%
HF hospitalizations per dose group	22%	17%	14%	11%	9%	8%
Odds ratio of HF hospitalizations (95% CI)	ref	0.71 (0.48-1.06)p=0.0974	0.59 (0.42-0.85)p=0.0043	0.47 (0.33-0.68)p<0.0001	0.44 (0.32-0.62)p<0.0001	0.42 (0.21-0.84)p=0.0137
KM rate per dose group	17%	11%	10%	7%	5%	5%
Hazard ratio for death (95% CI)	ref	0.66 (0.42-1.05)p=0.0780	0.55 (0.36-0.84)p=0.0060	0.35 (0.22-0.54)p<0.0001	0.25 (0.18-0.39)p<0.0001	0.38 (0.16-0.93)p=0.034

ref = referent group for Odds Ratio and Hazard Ratio is the 0 mg dose group
KM rate = Kaplan-Meier rate for all-cause mortality

Conclusions: Carvedilol dose in the community appears lower than in RCT, is influenced by NYHA functional class and tends to be higher when prescribed by cardiologists. At all doses, patients taking carvedilol have a lower incidence of death and heart failure hospitalization than those not receiving drug. This study demonstrates the utility of beta-blocker therapy in the community and also confirms the RCT findings that lower doses of carvedilol can also provide clinical benefit in the usual care setting.

2:45 p.m.

821-4 Beta-Blockers Reduce Heart Failure Mortality Regardless of the Initial Heart Rate: Data From the ICONS Study

Jonathan G. Howlett, David E. Johnstone, Jafna L. Cox, Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada

Background: The role of heart rate reduction as a mechanism of beta blockade (BB) effect in reduction of heart failure (HF) mortality is unknown. We sought to determine whether the mortality effect of BB was related to initial heart rate in hospitalized HF patients.
Methods: We utilized a prospective registry-based disease management database, the Improving Cardiovascular Outcomes in Nova Scotia (ICONS) study, to identify individuals with a discharge diagnosis of HF from any Nova Scotia hospital between October 15, 1997 and July 1, 2000. Patients were stratified according to their admission heart rate quintiles in beats/min, (> 115, 100-115, 86-99, 72-85,<72). Variables were recorded prospectively and censored at 2 years.
Results: There were 4888 unique patients, with average age of 76 years; 52% were female. Patients prescribed BB were younger (age 74 vs. 77), with lower creatinine (133 vs. 143 umol/L) and higher EF (43% vs. 38%). After adjustment for co-morbid conditions, hazard ratios for mortality with BB at two years were determined:

Initial Heart Rate (beats/min)	Hazard Ratio	95% CI	p Value
> 115 (n=990)	0.54	0.42- 0.71	0.0001
100-115 (n=1006)	0.62	0.47- 0.80	0.0003
86-99 (n=977)	0.57	0.44 - 0.75	0.0001
72-85 (n=1015)	0.61	0.47-0.79	0.0002
< 72 (n=900)	0.69	0.52- 0.92	0.002

Beta blocker prescription at discharge was associated with 37% lower two year mortality (31% vs. 42%). This finding was consistent regardless of heart rate quintile. The hazard ratio for BB in those with heart rate <65 bpm was 0.71, p= 0.09.
Conclusion: Beta blockers reduce mortality in unselected patients discharged from hospital with HF regardless of their admission heart rate. Further data is required in those with severe bradycardia.

3:00 p.m.

821-5 Risks of Death and Hospitalization in Heart Failure Patients Receiving Carvedilol Versus Metoprolol Tartrate: A Retrospective Claims-Based Study

Thomas E. Delea, Richard H. Stanford, May Hagiwara, John S. Edelsberg, Gerry Oster, Policy Analysis Inc., Brookline, MA, GlaxoSmithKline, Research Triangle Park, NC

Background: The Carvedilol or Metoprolol European Trial (COMET) demonstrated improved survival with carvedilol (C) versus metoprolol tartrate (MT) in patients with heart failure. The benefits of C versus MT in heart failure patients in typical US clinical practice are unknown.
Methods: Using a large US health-insurance claims database linked to mortality information from the US Social Security Administration, we compared the risks of death and hospitalization and the costs of inpatient care in heart failure patients receiving C versus MT. Subjects included all persons with ≥1 prescription for either C or MT (but not both) from 9/97-8/00 who, within 12 months of their first prescription for C or MT, had: (1) ≥1 medical encounter with a primary diagnosis of heart failure; (2) ≥1 prescription for a loop diuretic; (3) ≥1 prescription for an angiotensin-converting enzyme inhibitor; (4) no prescriptions for a beta-blocker; and (5) continuous eligibility for health benefits.
Results: A total of 887 C patients and (coincidentally) an equal number of MT patients met all criteria for inclusion in the study. Mean follow-up was 11 months (maximum, 36 months). Mean dose prescribed (mg/day supplied) was 24 for C and 70 for MT; mean dose received (mg/day of follow-up) was only 14 for C and 44 for MT. C patients were younger, more likely to be men, seen by a cardiologist, and prescribed digoxin; they also had higher pretreatment heart failure costs. However, they were less likely to have hypertension or other cardiovascular disease, and also had lower pretreatment cardiovascular costs. Controlling for these differences using Cox proportional hazards regression, receipt of C versus MT was associated with reduced risk of all-cause mortality (hazard ratio .78; 95% CI .61-.99) and all-cause hospitalization (hazard ratio .76; 95% CI .66-.89). In a propensity-matched sample of C and MT patients (n=562 each), expected costs of cardiovascular inpatient care at 36 months were $6,164 lower for C than MT (95% CI $1,330-$10,714).
Conclusion: Consistent with findings from COMET, our results suggest that C improves survival and reduces costs of care compared with MT in heart failure patients in typical US clinical practice.

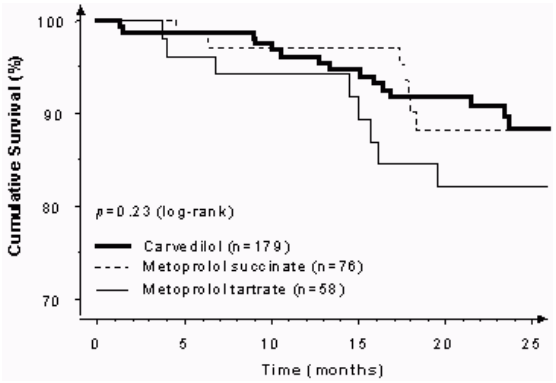
3:15 p.m.

821-6 Beta-Blocker Utilization in Patients With Heart Failure: A Single-Center, Two-Year Follow-Up

Anoop Parameswaran, W. H. Wilson Tang, Gary S. Francis, Ritesh Gupta, James B. Young, Cleveland Clinic Foundation, Cleveland, OH

Background: The longitudinal pattern of beta-blocker (BB) utilization in a heart failure (HF) practice setting has not been explored. Studies have not addressed the use of BB over time to determine the "target" rates of use and reasons for discontinuation.
Methods: We reviewed consecutive patients with a clinical diagnosis of HF seen in a specialized HF clinic between 3/01-5/01, and determined the pattern of BB utilization and clinical outcomes over a subsequent 2-year period.
Results: From a cohort of 496 patients (mean age 61±14 years, 60% male, 53% with ischemic etiology, mean LVEF 28±15%), 75% had a trial with a BB. On follow-up at 6, 12, and 24 months, BB utilization rates were maintained at 69%, 70% and 67%, respectively. Of the 120 non-BB users, 28 (23%) were subsequently initiated on BB, despite known relative contraindications in 53% of patients. In 2 years, the discontinuation rate was 10%, and the most common reason for discontinuation was failure to restart BB following hospitalization (31%). In this non-randomized cohort, the 2-year all-cause mortality was comparable among different BBs (Figure).
Conclusion: Utilization rates of BB in our HF clinic remain constant (67-70%) throughout a 2-year follow-up and likely represents a reasonable "target". Of those who discontinued

BB, 31% were due to failure to restart BB following hospitalization. More vigilance regarding restoration of BB usage following hospital discharge is in order.



POSTER SESSION

1108 Heart Failure: Outcomes II

Monday, March 08, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 4:00 p.m.-5:00 p.m.

1108-109 Low Hemoglobin Is an Independent Predictor of Adverse Fatal and Nonfatal Outcomes in Both Reduced and Preserved Systolic Function Chronic Heart Failure: Findings From the Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity Program (CHARM)

John J. McMurray, Chim C. Lang, Karl Swedberg, Jan Östergren, Christopher B. Granger, Eric Michelson, James B. Young, Bertil Olofsson, Mark Dunlap, Salim Yusuf, Marc A. Pfeffer, for the CHARM Investigators, Western Infirmary, Glasgow, United Kingdom

Background: Low hemoglobin (Hb) is associated with higher mortality in patients with chronic heart failure (CHF) and a reduced left ventricular ejection fraction (LVEF). Whether Hb is an *independent* predictor of survival and also predicts non-fatal outcomes is unclear. The importance of Hb in CHF and preserved LVEF is unknown.
Methods: The 3 CHARM trials were: i) CHARM-Alternative (n= 2028): LVEF ≤ 0.40 intolerant of an ACE inhibitor (ACE-I) ii) CHARM-Added (n=2548): LVEF ≤ 0.40 taking an ACE-I iii) CHARM-Preserved (n=3025): LVEF > 0.40. Patients were randomised to placebo or candesartan and followed for 37.7 months. Outcomes were compared in those with Hb ≤ and > median (13.6g/dL).
Results: Unadjusted outcomes are shown in the table. In a multivariate analysis Hb was an independent predictor of outcomes in both reduced LVEF and preserved LVEF CHF. For the 2 low LVEF trials combined, the hazard ratios (HR) for > median versus ≤ median Hb were: Death 0.62 95% CI (0.51-0.75) p<0.0001; CHF hospitalization 0.72 (0.60-0.86) p=0.0005 and death or CHF hospitalization 0.68 (0.58-0.78) p<0.0001. For CHARM-Preserved the HR were: 0.63 (0.46-0.86) p=0.004, 0.62 (0.47-0.81) p=0.0005 and 0.65 (0.52-0.81) p=0.0002, respectively.
Outcome in overall CHARM Programme according to whether baseline haemoglobin was above or equal to/below median

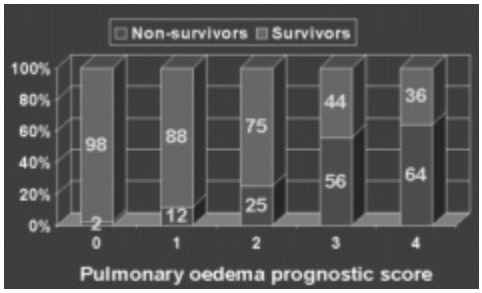
	Hb > median (n=1368)	Hb ≤ median (n=1281)
Outcome (%)		
death	19.0	27.9
CHF hospitalization	22.5	30.3
Death or CHF hospitalization	33.5	44.9

Conclusion: Hb is an independent predictor not only of death but also of CHF hospitalization. Hb is of as much prognostic significance in CHF with preserved LVEF as in CHF with a reduced LVEF.

1108-110 Pulmonary Edema Prognostic Score: A Novel Simple Prognostic Tool for Short-Term Events in Acute Cardiogenic Pulmonary Edema

Marcin Fiutowski, Tomasz Waszyrowski, Maria Krzeminska-Pakula, Jaroslaw D. Kasprzak, Medical University of Lodz, Lodz, Poland, Jonscher Hospital, Lodz, Poland

BACKGROUND: Cardiogenic pulmonary edema (CPE) is a common reason of hospitalisation connected with high mortality, but few data are published regarding long- and short-term prognosis and no prognostic scales are in use.
AIM: To establish a simple score predicting the in-hospital prognosis in patients with CPE.
METHODS AND RESULTS: We studied 276 Pts (148 females; mean age 70 years) hospitalised due to CPO (hospital stay 12±7 days). In-hospital mortality was 21%. 44 clinical variables were included in the analysis to revealthe most significant mortality predictors: acute myocardial infarction (RR=2,12), heart rate:>115/min. (RR=2,13), systolic blood pressure ≤ 130mmHg (RR=3,61) and white blood cells>11500/mm^3 (RR=2,26) on presentation. The number of risk factors was summed to create pulmonary edema prognostic score (PEPS). PEPS had a linear relationship with mortality - figure. Pts with PEPS 0 had very good short-term prognosis with 2% in-hospital mortality rate (RR=0,07) whereas mortality in Pts with PEPS 4 was 64% (RR=3,31). Receiver operating characteristic curve analysis proved good discriminative ability (AUC= 0,78). Score above 1 had sensitivity of 79%, specificity of 62%, 36% positive and 92% negative predictive value for in-hospital mortality
CONCLUSIONS: Pulmonary edema prognostic score is a simple bedside tool allowing a precise prediction of in-hospital prognosis after acute cardiogenic pulmonary edema.



1108-111 Serum Hyaluronic Acid Elevation in Patients With Decompensated Congestive Heart Failure Is Independent of Left Ventricular Systolic Function

Leonardo C. Clavijo, Daniel J. Cantillon, Jinguo Chen, Lurong Zhang, Michael D. Greenberg, Cynthia M. Tracy, Georgetown University, Washington, DC

BACKGROUND: Hyaluronic acid (HA), an extracellular glycosaminoglycan, is elevated during hepatic hypoperfusion, edema and fibroproliferative disorders. Serum HA is 90% metabolized and excreted by the liver. We have recently demonstrated that serum HA is elevated in patients (pts) with decompensated CHF (dCHF).
HYPOTHESIS: Serum HA elevation in pts with clinically dCHF is independent of LV systolic function (LVSF) and CHF etiology (ischemic vs. non-ischemic), thus reflecting poor hepatic perfusion and edema.
METHODS: A novel enzyme linked immunosorbent assay (ELISA) was used to measure serum HA levels in two hundred pts consecutively admitted to the hospital. Fourteen pts were excluded due to chronic liver disease or renal insufficiency. All dCHF pts were symptomatic and the diagnosis confirmed by a cardiologist blinded to HA level. Based on LVSF measured by echocardiogram, gated nuclear imaging or ventriculogram dCHF pts were divided in two groups: dCHF + preserved LVSF (EF>40%) or dCHF + depressed LVSF (EF <40%). Ischemic cardiomyopathy was identified by the presence or absence of coronary disease in the setting of dCHF.
RESULTS: Admission serum HA levels were markedly elevated in pts with dCHF (259.0 ng/ml, SEM=49.5, n=32) vs. non-CHF pts (104.0 ng/ml, SEM=6.2, n=154), p<0.001. Serum HA levels in pts with dCHF + preserved LVSF (348.5 ng/ml, SEM=106.2, n=14) and dCHF + depressed LVF (189.4 ng/ml, SEM=24.4, n=18) were elevated compare to non-CHF pts (104.0 ng/ml, SEM=6.2, n=154), p<0.001. The difference between dCHF with preserved and depressed LVSF was not significant (p=0.11). There was no difference in HA levels between ischemic and non-ischemic dCHF groups (293.3 ng/ml, SEM=71.9, n=21 vs. 193.3 ng/ml, SEM=41.3, n=11), p=0.27.
CONCLUSION: Serum hyaluronic acid level is elevated in pts with symptomatic clinically dCHF. HA elevation is independent of left ventricular systolic function and ischemic etiology. Further studies are needed to investigate the mechanisms and prognostic value of HA elevation during dCHF.

1108-112 An Embolic Event to Death in More Than 50 Percent of Patients With Idiopathic Dilated Cardiomyopathy in End-Stage Heart Failure

Antonio C. Barretto, Sr., Mucio T. Oliveira Jr, Sr., Robinson T. Munhoz, Sr., Airton R. Scipioni, Sr., Maria L. Higuchi, Jose A F Ramires, Sr., Heart Institute, (InCor), University of São Paulo Medical School, São Paulo, Brazil

Background: Pts with idiopathic dilated cardiomyopathy (IDC) and end stage heart failure has a worse prognosis with high mortality. Embolic events (EE) could contribute to the heart failure bad evolution of these pts.
Objective: To clarify the importance of EE in the evolution of pts with IDC, we analyzed the data from necropsies of heart failure pts that died at the hospital in the last ten years.
Methods: Between 1990 and 1999, 3847 necropsies were performed and 118 pts had IDC. The pts mean age was 41.8 years and 74 (62,7%) were male. The echocardiogram showed a mean LV end diastolic diameter of 76,0 mm and a mean LV ejection fraction of 0,32. Results: EE were identified in 90 (76,3%) pts, 61 (51,7%) of those had pulmonary embolism (PE), 29 (24,6%) systemic embolism (SE) and 33 (14.2%) both. The great majority of EE was not diagnosis in life. Cardiac thrombus was detected in right chambers in 26 pts (22,0%) and in left chambers in 18 (24,62%). The main embolic source